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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/626,731	07/27/2000	Man Sung Co	GNN-5315DV2	5819

7590

10/07/2002

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EXAMINER

GAMBEL, PHILLIP

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 10/07/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. <u>09/626731</u>	Applicant(s) <u>CO ET AL.</u>	
	Examiner <u>Gambel</u>	Art Unit <u>1644</u>	

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 7/26/01

2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-10 is/are pending in the application.

 4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-10 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

1. Applicant's amendment, filed 7/26/02 (Paper No. 14), has been entered.
Claims 1 and 9 have been amended.

Claims 1-10 are under consideration in the instant application.

2. This Office Action will be in response to applicant's arguments, filed 7/26/02 (Paper No. 14).
The rejections of record can be found in the previous Office Action (Paper No. 10).
3. Formal drawings submitted 7/26/02 comply with 37 CFR 1.84.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined *under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e))*.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Upon reconsideration applicant's amended claims and arguments, filed 7/26/02 (Paper No. 14), the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Freeman et al. (U.S. Patent No. 6,130,316) as it applies to the instant claims have been withdrawn.

7. Claims 1-10 are rejected under 35 U.S.C. § 102(b) as being anticipated by Blazar et al. (WO 95/34320) (1449) (see entire document) essentially for the reasons of record.

Applicant's amended claims and arguments, filed 7/26/02 (Paper No. 14), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that Blazar et al. do not teach contacting the donor cells with B7-1-specific / B7-2-specific antibodies and recipient cells from the patient for a period of time of "from about 1 to about 48 hours before being introduced into the patient".

Although applicant points to page 28, lines 20-32 for the teaching of incubating donor and recipient cells with antibodies for about 2.5 to 4 days by Blazar et al., Blazar et al. teach saturating B7 with inhibitors such as hCTLA-4-Ig and anti-LFA-1 for 3 hours (see pages 28-29, overlapping paragraph). Therefore, Blazar et al. does teach saturating B7 with inhibitors with the newly added claimed limitations (e.g. 3 hours).

Again, Blazar et al. teach the use of inhibitors including those that bind both B7-1 and B7-2 (e.g. Summary of the Invention, including page 4, paragraph 1; Detailed Description of the Invention, including page 6 - page 7, paragraph 1, page 17, paragraph 1 and Uses of the Invention, page 11, paragraph) to induce T cell unresponsiveness for bone marrow transplantation, including its use for the treatment of hematological malignancies and anemia (e.g. see Background of the Invention, Summary of the Invention and Uses of the Invention). In addition, Blazar et al. teach the inhibitory agents can be administered for 18-36 hours after T cell priming e.g. see page 23, paragraph 1). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. Bone marrow comprise lymphocytes, stem cells and immature blood cells. The claimed functional limitations and constructions encompassed by the claims would be inherent properties of the referenced methods to induce T cell responsiveness with B7-1 and B7-2-specific antibodies for bone marrow transplantation in the treatment of malignancies and anemia.

Applicant's arguments are not found persuasive.

8. Claims 1-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Blazar et al. (WO 95/34320) (1449) alone or in combination with Chappel et al. (U.S. Patent No. 6,096,537).

As indicated previously and above, Blazar et al. teach the use of inhibitors including those that bind both B7-1 and B7-2 (e.g. Summary of the Invention, including page 4, paragraph 1; Detailed Description of the Invention, including page 6 - page 7, paragraph 1, page 17, paragraph 1 and Uses of the Invention, page 11, paragraph) to induce T cell unresponsiveness for bone marrow transplantation, including its use for the treatment of hematological malignancies and anemia (e.g. see Background of the Invention, Summary of the Invention and Uses of the Invention). In addition, Blazar et al. teach the inhibitory agents can be administered for 18-36 hours after T cell priming e.g. see page 23, paragraph 1). Bone marrow comprise lymphocytes, stem cells and immature blood cells. The claimed functional limitations and constructions encompassed by the claims would be intrinsic properties of the referenced methods to induce T cell responsiveness with B7-1 and B7-2-specific antibodies for bone marrow transplantation in the treatment of malignancies and anemia.

Although applicant points to page 28, lines 20-32 for the teaching of incubating donor and recipient cells with antibodies for about 2.5 to 4 days by Blazar et al., Blazar et al. teach saturating B7 with inhibitors such as hCTLA-4-Ig and anti-LFA-1 for 3 hours (see pages 28-29, overlapping paragraph and Experiment 3 on page 31). Therefore, Blazar et al. does teach saturating B7 with inhibitors with the newly added claimed limitations (e.g. 3 hours).

Blazar et al. differs from the claimed methods by not disclosing the range of about 1- 24 hours per se. Given the teaching of Blazar et al., including saturating B7 with inhibitors such as hCTLA-4-Ig and anti-LFA-1 for 3 hours (see pages 28-29, overlapping paragraph and Experiment 3 on page 31). It is noted that Experiment 3 on page 31 discloses that the inclusion of the priming step in the treatment regimen can increase the inhibitory effects of the agents.

Given the teaching of Blazar et al. that the in vitro incubation step with agents that block B7 factors the development of donor anti-host specific hyporesponsiveness (In vitro incubation of splenocytes with agents on pages 28-29) with the example of 3 hours (pages 28-29 and 31), one of ordinary skill in the art would be motivated to select those times of incubating donor cells with B7-specific inhibitors to achieve donor anti-host specific hyporesponsiveness, consistent with the claimed therapeutic endpoints. One of ordinary skill in the art would have appreciated that various times in including times of about 1 -24 hours would have been suitable depending on the nature of the donor cells and the nature of the agents and conditions suitable to achieve donor anti-host specific hyporesponsiveness.

In addition, it is noted that Chappel et al. teach masking antigens to achieve or to induce immunological nonresponsiveness can be for 30 minutes (see entire document, including column 8, paragraph 1 and column 18, paragraph 1), which reads on "about 1 hour" of the claimed methods. It is

noted that Chappel et al. Exemplify masking murine pancreatic islet cells and not the mixture of cells taught by Blazar et al. Or that encompassed by the claimed methods.

Again, given the prior art teachings of Blazar et al. and Chappel et al., one of ordinary would have been motivated to pretreat donor cells for a period of time to achieve or to induce donor anti-host specific hyporesponsiveness. Given such teachings, one of ordinary skill in the art would have expected that a range of times, including that encompassed by the claimed "about 1-24 hours" would have been met at the time the invention was made given the nature of the donor cells, the. Given the teachings of the prior art references, including the Examples described by Blazar et al. And Chappel et al, one of ordinary skill in the art would have appreciated that achieving immunological nonresponsiveness by pretreating donor cells with B7-specific inhibitors would have varied depending on the nature of the donor cells, the nature of the agents and the conditions suitable for achieving said immunological nonresponsiveness. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention, including a range of "about 1 - 24 hours" or pretreating donor cells with B7-specific inhibitors to achieve immunological nonresponsiveness. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

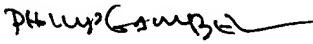
9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

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Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.



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Technology Center 1600
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